REMARKS

Claims 60-96 are pending in the captioned application. Claims 60-67 are allowed. Claims 68, 81, 90, 93, 95, and 96 have been amended and claims 69, 71, 74, 75, 79, 80, 82, 84, 87-89, 92, and 94 have been canceled without prejudice to applicant's right to pursue the canceled subject matter in this or other applications. Claim 90 has been amended to delete recitation of certain enzymes. Claims 68, 81, 93, 95, and 96 have been amended to indicate the origin of enzyme encoding sequences. Support for these amendments is found in the specification at the paragraph abridging page 5 and 6. These amendments do not introduce new matter.

Applicant respectfully requests that the amendments and remarks made herein be entered into the record of the instant application.

Rejection Under 35 U.S.C. § 112, First Paragraph, for Lack of Written Description

The Examiner has rejected claims 68-96 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. In particular, the Examiner contends that no guidance has been provided for the isolation or characterization of pyruvate kinase, acid invertase, starch synthase, 6-phosphofructokinase, sucrose synthase, and sucrose phosphate synthetase from any source, for the isolation and characterization of their corresponding genes, or for plant transformation with such genes.

To fulfill the written description requirement of Section 112, it is well settled that the invention must described in such detail that one skilled in the art would conclude that the inventor was in possession of the invention. *Regents of Univ. Cal. v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997). There is no particular form that the written description must take. The written description can be satisfied by disclosure in the specification or the drawings. *Vas-Cath*, 935 F.2d at 1559-1560. And, the written description inquiry turns on the knowledge of one of skill in the art:

> Since its inception, the Court of Appeals for the Federal Circuit has frequently addressed the "written description" requirement of § 112. A fairly uniform standard for determining compliance with the "written description" requirement has been maintained throughout: "Although [the applicant] does not have to describe exactly the subject matter claimed,... the

> description must clearly allow person of ordinary skill in the art to recognize that [he or she] invented what is claimed. *In re Gosteli*, 872 F.2d 1008, 1012 (Fed. Cir. 1989) (citations omitted; footnote omitted).

Vas-Cath, 935 F.2d at 1562-1563.

The criteria for determining sufficiency of written description set forth in Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112 ¶ 1, "Written Description" Requirement" ("the Guidelines") (published in the January 5, 2001 Federal Register at Volume 66, Number 4, pages 1099-1111), specifies that:

> Whether the specification shows that applicant was in possession of the claimed invention is not a single, simple determination, but rather is a factual determination reached by considering a number of factors. Factors to be considered in determining whether there is sufficient evidenced of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function and the method of making the claimed invention.
>
> *Id.* at page 1106, column 2, lines 25-41.

Where the specification discloses any relevant identifying characteristics, *i.e.*, physical, chemical and/or functional characteristics, sufficient to allow a skilled artisan to recognize the applicant was in possession of the claimed invention, a rejection for lack of written description under Section 112, first paragraph, is misplaced.

Furthermore, in accord with the Written Description Guidelines, what is conventional or well known to one of skill in the art need not be disclosed in detail and where the level of knowledge and skill in the art is high a written description questions should not be raised (Fed. Reg. Vol. 66, no. 4, January 5, 2001, p. 1106).

Claims 68, 81, 93, 95, and 96 have been amended to delete starch synthase, 6-phosphofructokinase (pyrophosphate), and sucrose phosphate synthetase. Claims 68, 81, 93, 95, and 96 have also been amended to indicate the source of the enzyme encoding sequences, including pyruvate kinase from *E. coli*, yeast, or potato, acid invertase from yeast, and sucrose synthase from potato. The specification clearly teaches that the nucleic acid sequences encoding enzymes used in the methods of the invention can originate from *E. coli*, yeast, or potato. See abridging paragraph pages 5 and 6.

The specification also teaches specific Enzyme Commission (EC) numbers for pyruvate kinase (EC 2.7.1.40), acid invertase (EC 3.2.1.26), and sucrose synthase (EC

2.4.1.13). The numbers are not general, but specific references to the function and structure of the particular enzymes. Moreover, the EC numbers represent an abbreviated way to reference available purified enzymes and sequences encoding the enzymes from particular species such as *E. coli*, yeast, or potato. For example, nucleic acids encoding pyruvate kinase (EC 2.7.1.40) had been isolated and the sequences were known in the art at the time of filing: Ohara et al., 1989 (bacteria genomic DNA sequence), IDS Ref No.: C12; Burke et al., 1983 (fungi genomic DNA sequence), IDS Ref No.: C02; and Blakeley et al., 1990 (plant cDNA sequence), IDS Ref No.: C01). Nucleic acids encoding acid invertase (EC 3.2.1.26) had been isolated and their sequences were known in the art at the time of filing: Taussig et al., 1983 (yeast DNA sequence), IDS Ref No.: C16; and Martin et al., 1987 (bacteria DNA sequence), IDS Ref No.: C10. Nucleic acids encoding sucrose synthase (EC 2.4.1.13) had been isolated and their sequences were known in the art at the time of filing (Salanoubat et al., 1987 (plant cDNA sequence), IDS Ref No.: C15).

The Examiner contends that the present situation is eminently analogous to the Eli Lilly case. *University of California v. Eli Lilly and Co.*, 199 F.3d 1559, 1559, 1568; 43 U.S.P.Q.2d 1398, 1406 (Fed. Cir. 1997). In the Eli Lilly case, the patentee had claimed a genus of sequences with a particular function while disclosing only one sequence and other sequences in the genus were not known in the art. In contrast, the present claims, as amended, are not claiming methods that encompass the use of unknown sequences, but rather known sequences that were available and were referenced in the specification by specific EC numbers.

The combination of specifying the origin of the encoding sequences and reference in the specification to the corresponding EC numbers provides adequate written description of the sequences used in the methods of the invention. The EC numbers disclosed in the specification are descriptions of the functional properties of the enzymes. The EC numbers in combination with the origin of the enzyme encoding sequences provides a reference to specific known encoding sequences. Applicant submits that the level of knowledge and skill in the art was sufficient that one would have recognized that Applicant possessed use of these known sequences. For example, see Blakeley et al., 1990 (plant cDNA sequence), IDS Ref No.: C01, and Ohara et al., 1989 (bacteria genomic DNA sequence), IDS Ref No.: C12, where the nucleic acid sequences encoding certain enzymes are referenced by and correlated to EC numbers. In accordance with the written description guidelines and case law, where the level of skill in the art is high, one need not describe what is known in detail. The combined description of EC numbers and origins is sufficient, such

that one skilled in the art would realize that the applicant was in possession of the glycolytic enzyme encoding sequences used in the methods of the invention.

Rejection Under 35 U.S.C. § 112, First Paragraph, for Lack of Enablement

The Examiner has rejected claims 68-96 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

In particular, the Examiner contends that the Coates declaration, submitted August 20, 2003, and the Burrell declarations, submitted July 14, 2003, rely upon antisense constructs or multiple sense constructs. Applicant respectfully submits that the Examiner is in error. The Examiner's attention is invited to paragraph 9 of the Coates declaration where transgenic plants engineered to express sucrose synthase in the sense direction and not in a multiple sense or anti-sense construct are described. Paragraph 11 of the Coates declaration clearly describes transgenic plants engineered to express pyruvate kinase in the sense direction and not in a multiple sense or anti-sense construct. The Burrell declaration dated February 25, 1997 (the "second Burrell declaration") describes an experiment in paragraphs 7 and 8 where transgenic plants were engineered to express sucrose synthase in the sense orientation and not in a multiple sense or anti-sense construct are described. With respect to claim 90, the fourth experiment described in paragraph 12 of the Coates declaration describes transgenic plants engineered to express pyruvate kinase and phosphofructokinase. Thus, contrary to the Examiner's contention, the declarations of Coates and Burrell demonstrate that the claimed methods, as amended, can be used in accordance with the teachings of the specification to successfully produce transgenic plants.

The Examiner also contends that the Coates and Burrell declarations rely upon particular genes that were not disclosed in the instant application. The particular genes, *i.e.*, pyruvate kinase from *E. coli*, yeast or potato, acid invertase from yeast, and sucrose synthase from potato are adequately described in the specification. Applicant respectfully disagrees for the reasons presented above in response to the written description rejection.

Regarding von Schaewen et al., the Examiner has maintained that the reference demonstrates the unpredictability inherent in plant transformation. According to the Examiner, the results of von Schaewen with respect to tobacco transformed to

overexpress a fusion invertase protein into cell walls demonstrate deleterious effects on plant health, and less appreciable, though notable, discoloration of leaves in transformed *Arabidopsis* plants. The Examiner also contends that the specification is silent with regard to the use or choice of any signal sequence. Applicant respectfully disagrees for the reasons below.

The objective of von Schaewen et al. was to alter source sink relationships to gain insight into principles governing the interaction. See page 3034, first column, first paragraph. Von Schaewen generated plants that express a yeast invertase gene in source organs, *i.e.*, mature leaves, and targeting expression to cell walls where invertase is not typically found. Upon observing deleterious effects, one skilled in the art would clearly recognize that the deleterious effects were caused by mis-expression and would be able to avoid or reduce such expression, without resorting to undue experimentation, by targeting plant tissues or cells where expression is normally found. Thus, one skilled in the art reading von Schaewen et al. would have known not to express invertase in source organs to avoid deleterious effects. The specification teaches specific regulatory elements including the patatin promoter that would lead to cytoplasmic expression or overexpression of a glycolytic enzyme in an appropriate location such as a sink organ. See page 4, lines 11-22. One skilled in the art following the teachings of the specification could have expressed a gene encoding a glycolytic enzyme in plant cells using a promoter such as the patatin promoter and avoid the deleterious effect.

Moreover, von Schaewen et al. examine leaves which are described as sink organs during early development and sources later in development. See page 3033, second column first full paragraph. In Fig. 5D of von Schaewen et al., leaves of varying stages of development from transgenic plants overexpressing invertase in cell walls are shown. It is clear that young leaves (sinks) do not exhibit deleterious phenotypes, whereas older mature leaves (sources) exhibit deleterious phenotypes. von Schaewen et al. also teach that the metabolic intermediate sucrose is essential to the source-sink interaction because it is produced in the leaves (sources) and transported to sinks and the extracellular expression of invertase would disrupt this transport. Abridging paragraph pages 3033 and 3034. von Schaewen et al. provides no evidence of the unpredictability of expressing a glycolytic enzyme in strong sinks such as tubers. Given the teaching of the specification, one skilled in the art would clearly be able to avoid the deleterious effects observed by von Schaewen et al. in mature leaves (sources). The skilled artisan would understand that expression of glycolytic enzymes in strong sinks such as tubers would not result in the same problems as observed in

leaves. The specification provides an example of such targeting at page 12, second paragraph, where plants transformed with a chimeric gene comprising PFK operably linked to a tuber specific promoter are disclosed. Thus, the skilled artisan could easily avoid the predicable deleterious effects observed by von Schaewen et al. simply by expressing glycolytic enzymes intracellularly or in sink organs as demonstrated in the specification.

In view of the forgoing amendments and reasoning, Applicant respectfully requests withdrawal of the rejections under 35 U.S.C. § 112, first paragraph.

CONCLUSION

Applicant respectfully requests entry and consideration of the foregoing amendments and remarks. No new matter has been introduced. The claims are believed to be free of the art and patentable. Withdrawal of all of the rejections and an early allowance is earnestly sought.

Respectfully submitted,

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Enclosure